The Spectrum of Serous Cystadenoma of the Pancreas

Clinical, Pathologic, and Surgical Aspects

CHRISTOPHER M. PYKE, M.B., F.R.A.C.S.,* JON A. VAN HEERDEN, M.D., F.R.C.S.(C), F.A.C.S.,* THOMAS V. COLBY, M.D.,†, MICHAEL G. SARR, M.D.,* and AMY L. WEAVER, M.S.‡

Serous cystadenoma of the pancreas is a rare lesion thought to be almost invariably benign. Since 1978, 211 cases have been reported in the literature. Some have been recognized by computed tomography (CT) when small and asymptomatic. The authors have reviewed their experience with 40 patients (median follow-up of 1.9 years, maximum of 22.2 years) from 1936 to 1991. One third (13) were asymptomatic, of whom eight (20%) were discovered intraoperatively. Of those 20 who had CT, an unequivocal preoperative diagnosis was reached in none. Needle biopsy proved accurate in two patients. Endoscopic retrograde cholangiopancreatography (ERCP) and biopsy were performed with diagnostic success on one occasion. Three patients presented acutely. The tumor was resected in 90%, with an operative mortality rate of 10%. Enucleation of the tumor without formal anatomic pancreatectomy necessitated reoperation for complications in four of eight patients. Survival after successful resection paralleled expected survival. Serous cystadenoma may be associated with von Hippel–Lindau syndrome. The current role for conservative management remains questionable because of our current inability to reliably differentiate many of these benign neoplasms from malignant cystic neoplasms of the pancreas.

From the Departments of Surgery, Pathology,† and Biostatistics,‡ Mayo Clinic and Mayo Foundation, Rochester, Minnesota*

SEROUS CYSTADENOMA OF the pancreas (synonym: microcystic adenoma, glycogen-rich adenoma) occupies a unique place among cystic tumors of the pancreas because it has little or no malignant potential.[1] With the advent of improvements in computed tomography (CT) and ultrasonographic imaging, a number of cystic lesions are being recognized with increasing frequency and must be considered clinically in the differential diagnosis of cystic neoplasms of the pancreas, including true congenital cysts, acquired cysts, and pseudocysts (Table 1).[2]

In the past, with the indolent nature of serous cystadenoma and the formidable morbidity and mortality rates of pancreatectomy, the prevailing therapeutic philosophy was that of judicious observation.[3,4] Considerable effort was expended in the accurate preoperative differentiation of serous cystadenoma *versus* mucinous cystadenocarcinoma via CT[5–8] and fine needle aspiration[3,9] with a view toward conservative management of the former. However, the recent decline in mortality rate after major pancreatic surgery,[10,11] the accumulating number of complications of serous cystadenomas[12–15] including the rare possibility of malignant transformation,[16] complications related to preoperative diagnostic procedures,[5,17] and most importantly the inability to confidently differentiate serous from mucinous neoplasms have changed the therapeutic philosophy of most surgeons to one of a more aggressive surgical approach.[4]

Our extensive experience with this group of patients addresses the potential weaknesses of nonoperative management, confirms the continuing excellent prognosis of serous cystadenoma, and acknowledges the possibility that many of these patients have associated multiple-system disease, as suggested previously.[3,12,13,15,18,19]

Materials and Methods

Forty patients with the diagnosis of serous cystadenoma of the pancreas were identified in the files of surgically resected and histologically verified benign pancreatic cystic tumors seen at the Mayo Clinic between 1936 and 1991, inclusive. Patients with polycystic pancreatic disease, whether part of von Hippel–Lindau disease or occurring sporadically, were excluded. All pathology specimens were reviewed and the diagnosis confirmed by one of the authors (TVC). Clinical presentation, operative treatment, and postoperative course were abstracted from the clinical

Address reprint requests to Jon A. van Heerden, M.D., Professor of Surgery, Department of Surgery, Mayo Medical School, 200 First St SW, Rochester, MN 55905.

Accepted for publication September 26, 1991.

TABLE 1. *Cysts and Cystic Neoplasms of the Pancreas*

- Cystic neoplasms
  - Benign (microcystic) serous cystadenoma
  - Benign and malignant mucinous (macrocystic) cystadenoma and cystadenocarcinoma
  - Acinar cell cystadenocarcinoma
  - Papillary–cystic epithelial neoplasm
  - Teratomatous cyst
  - Cystic choriocarcinoma
- Acquired cysts
  - Parasitic cysts
    - Echinococcus cyst (hydatid cyst)
    - Cyst caused by *Taenia solium* (tapeworm)
  - Pseudocysts
    - Cystic necrosis of the pancreas and peripancreatic tissues
    - Chronic pseudocyst
- Congenital true cysts
  - Single true cyst(s)
    - Polycystic disease of the pancreas without related anomolies
    - Pancreatic macrocysts associated with cystic fibrosis
    - Polycystic disease of the pancreas associated with cerebellar tumors and retinal angiomata (von Hippel–Lindau disease)
    - Pancreatic cysts associated with polycystic disease of kidneys (Potter, type I or II)
  - Enterogenous cysts
  - Dermoid cysts

records. Follow-up was obtained by death certificate, repeat examination, or by patient questionnaire with subsequent telephone interview. Twenty per cent (8/40) of the patients did not have recent (within 1 year) follow-up at the time of this study. These eight patients had been followed for a median of 2.5 years, with a range of 10 days to 22.2 years.

Patient survival was calculated using the Kaplan–Meier method[20] and compared with the expected survival for the 1980 West North Central population using the log-rank test.[21] Comparisons of continuous variables among two groups were made using the Wilcoxon rank sum Test.

Results

Clinical Presentation

There were 14 men and 26 women, with a mean age of 62.7 years (range, 35 to 84 years) (Fig. 1). Twenty-seven patients (69%) had symptoms believed related wholly or in part to local pressure effects of the cystic neoplasm (Table 2), including abdominal pain or mass, nausea and vomiting, and weight loss. Extrahepatic biliary obstruction was distinctly unusual (four patients—10%). Thirteen patients (33%) were completely asymptomatic, and the lesion was found either intraoperatively during celiotomy for another problem (eight patients) or preoperatively during evaluation of an unrelated disorder (five patients). The mean size of symptomatic lesions (7.5 cm; range, 1 to 25 cm) was not significantly different from the asymptomatic neoplasms (6 cm; range, 2 to 11 cm) (Table 3). One patient presented with an acute surgical abdomen. This was due to hemorrhage into the neoplasm

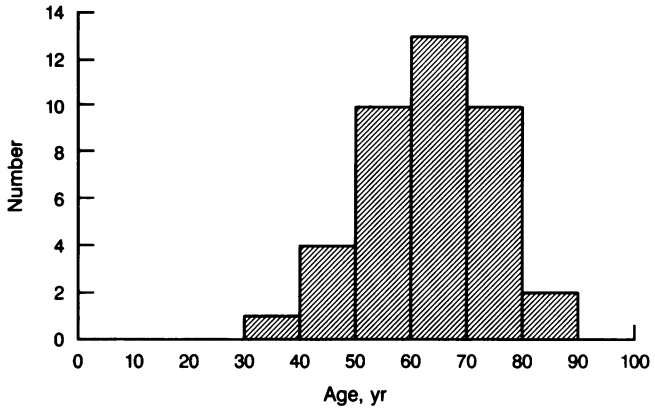

FIG. 1. Age (by decade) of 40 patients with serous cystadenoma of the pancreas.

with subsequent tumor rupture and hemoperitoneum. Two other patients presented with acute surgical situations, one with gastrointestinal bleeding from a duodenal ulcer, who was found to have a cystadenoma intraoperatively at the time of celiotomy, and another who had his tumor diagnosed during workup for an acute abdominal crisis caused by sickle cell disease.

Preoperative Diagnosis

The advent of CT and ultrasonography in 1974 allowed the possibility of objective preoperative imaging; before this, lesions were implicated by a palpable mass or a mass effect on contrast studies of the gastrointestinal tract. Since 1974, 20 patients had a preoperative CT that showed a cystic mass in every patient; although serous cystadenoma was stated to be the most likely diagnosis in 10, an unequivocal diagnosis was unable to be made in any patient. Ultrasonography was performed in 15 patients and showed a cystic mass in 12 of 15 (missing lesions 6 cm, 5.4 cm, and 3 cm), but it was pathognomonic of serous cystadenoma in none. Magnetic resonance imaging was

TABLE 2. *Clinical Presentation of Serous Cystadenoma of Pancreas*

Symptom/Sign	No. of Patients
Pain	18
Abdominal mass	12
Nausea, vomiting	8
Weight loss	6
Jaundice	4
Recurrent pancreatitis	2
Hemoperitoneum*	1
Melena†	1
Sickle cell crisis‡	1
None	13

* Bleeding into and rupture of neoplasm.
† Bleeding duodenal ulcer distant from serous cystadenoma.
‡ Serous cystadenoma found during workup of acute abdominal symptoms due to sickle cell crisis.

TABLE 3. *Serous Cystadenoma of the Pancreas*

Presentation	Size (cm)		
	Mean	Median	Range
Symptomatic (n = 27)	7.5	6.0	0.8–25.0
Incidental (n = 13)	6.0	6.0	2.0–11.0
Incidentally found by computed tomography before operation (5/13)	6.5	6.0	3.5–11.0

of no additional benefit (one patient). Preoperative needle biopsy was performed in one patient with an unequivocal positive diagnosis. One patient had biopsy at endoscopic retrograde cholangiopancreatography (ERCP) examination, which was highly suggestive. One patient had core needle biopsy during celiotomy for splenectomy, yielding an unequivocal positive result.

Within the group of patients who underwent celiotomy for a known pancreatic lesion (27 patients), none of the lesions was thought to represent pancreatic pseudocysts because of the clinical spectrum. Also, none had previously undergone an enteric drainage procedure because of a misdiagnosis of pancreatic pseudocyst. The tentative preoperative diagnosis was serous cystadenoma in 10 and various other lesions in the other 17 patients (Table 4).

Associated Diseases

Associations with other diseases were sought and are as listed in Table 5. Most common were cholelithiasis, diabetes mellitus, colonic polyps, and multinodular goiter. Two patients had pheochromocytomas.

Operative Findings/Treatments

The cystic neoplasms were located primarily in the pancreatic head in 17 patients, uncinate process in 5, neck in 3, body in 16, and in the tail in 6 (Seven patients had multiple tumor sites.). Two patients had separate, distinct serous cystadenomas. Operative treatment is shown in Table 6. Resection was carried out in 36 patients. Two tumors were deemed too large for safe resection and were bypassed. Two patients with presumptive serous cystadenomas underwent biopsy only. In the eight patients in whom the lesion was found incidentally during celiotomy, a number of other genitourinary, colorectal, gastric, and biliary procedures were carried out.

TABLE 4. *Serous Cystadenoma of the Pancreas: Presumed Preoperative Diagnosis (27 patients)**

Diagnosis	No. of Patients
Serous cystadenoma	10
Mucinous cystadenoma	3
Malignancy of unknown type	8
Benign cystic lesion of questionable type	4
Islet cell tumor	2

* Patients undergoing celiotomy for a known or presumed pancreatic mass.

TABLE 5. *Serous Cystadenoma of the Pancreas: Concomitant Disorders*

Disorder	No. of Patients
Cholelithiasis	11
Diabetes mellitus	7
Colonic polyps	6
Multinodular goiter	4
Peptic ulcer	2
Pheochromocytoma	2
Insulinoma	1
Chronic pancreatitis	1
Ampullary cancer	1
Colonic adenocarcinoma	1
Cirrhosis	1
Renal angiolipoma	1
Renal cysts	1
Renal stones	1
Macular degeneration	1
Hairy cell leukemia	1
Non-Hodgkin's lymphoma	1
Cancer of pharynx	1
Retroperitoneal fibrosis	1
Adenocarcinoma of cervix	1
α_1 antitrypsin deficiency	1
Hemangiomatosis of the small intestine	1
Sickle cell crisis	1
Papillary cancer of the thyroid	1

Surgical Results

Morbidity and Mortality Rates. Operative mortality rate was 10% (four patients); one died of pulmonary embolus and two of superior mesenteric artery occlusion. One patient who died suddenly on postoperative day 2 had no autopsy performed. Two of these patients had undergone enucleation, one a distal pancreatectomy and one a Whipple resection. Significant related postoperative complications occurred in 15 patients (38%). Pancreatic fistulas developed in six patients, two of whom had undergone enucleation. Both of these required reoperative treatment for management of the pancreatic fistula by conversion to distal pancreatectomy with pancreatojejunostomy for a distal lesion, and occlusion of the fistula

TABLE 6. *Serous Cystandenoma of the Pancreas: Operative Management*

Management	No. of Patients
Radical pancreatoduodenectomy	11
Distal pancreatectomy	17
Enucleation	8
Bypass	2
Biopsy*	2

* One too large for safe removal and one found during hysterectomy.

with methyl acrylate glue for a tumor in the head of the pancreas. One patient with a postoperative bile leak required revision hepaticojejunostomy. Other surgical problems requiring reoperation included a revision gastrojejunostomy for gastric stasis, cystoenteric drainage of a postoperative pancreatic pseudocyst, revision of a hepaticojejunostomy for stenosis, and conversion of an enucleated lesion in the head of the pancreas to a pancreatoduodenectomy for postoperative pancreatitis.

Survival. Prognosis in this group of patients was excellent. With a median follow-up postoperatively of 1.9 years (maximum of 22.2 years), 23 patients are still alive. After removing the six patients whom either died or were lost to follow-up within 30 days after surgery, the median survival was 16 years, with 2-, 5-, and 10-year survivals of 90%, 81%, and 64%, respectively (Fig. 2).

Discussion

The finding of a cystic lesion in the pancreas raises many controversial questions, especially when the clinical situation supports a diagnosis of serous cystadenoma. Can an accurate preoperative diagnosis be made to confidently differentiate the benign serous cystadenoma from its malignant counterpart, the mucinous cystadenocarcinoma? Should all cystic neoplasms of the pancreas be resected or can a more selective treatment policy be followed? What is the appropriate approach if such a lesion is found incidentally? And, is this neoplasm a marker for other diseases?

Before addressing these questions, one must understand the natural history of serous cystadenomas of the pancreas. In 1978, Compagno and Oertel[1] were the first to fully describe and differentiate pathologically serous from mucinous cystic neoplasms of the pancreas. This is a critical

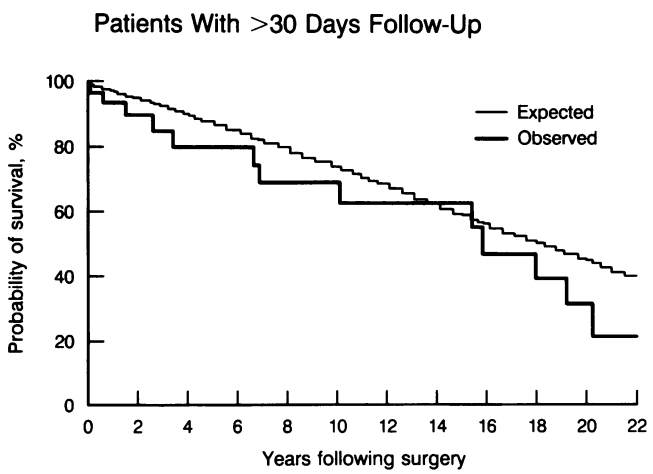

FIG. 2. Observed survival (Kaplan–Meier method) of patients with pancreatic serous cystadenoma of the pancreas compared with expected survival based on the WNC 1980 population.

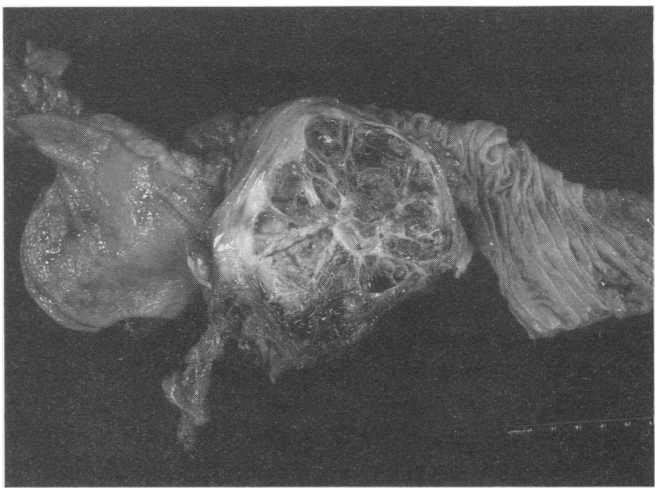

FIG. 3. Gross features of serous cystadenoma. In this specimen from a Whipple procedure, the microcystic adenoma of the head of the pancreas has been cut across to show the presence of gross cysts as well as stellate central scarring. The opened duodenum lies adjacent to the tumor.

distinction because serous cystadenomas are virtually always benign, whereas the mucinous variety of cystic neoplasms of the pancreas either carry a very real potential for malignant transformation or have transformed into *cystadenocarcinomas* at the time of presentation.[22] Since 1978, only one instance of malignant transformation of a serous cystadenoma[16] has been documented in more than 211 reported cases.[1,4,5,7,18,23] In the landmark paper that defines microcystic adenomas, Compagno and Oertel[1] also described one case that could be considered as malignant. Thus, malignant transformation of serous cystadenomas must be exceedingly unusual. Also, the indolent nature of this neoplasm is important, as demonstrated by one of our patients who was found to have a 3-cm, biopsy-confirmed serous cystadenoma of the pancreas at the time of splenectomy. This was followed by surveillance CT over the ensuing 8 years, by which time the lesion had reached a size of only 7 cm.

Can Serous Cystadenomas Be Confidently Differentiated From Their Malignant Counterpart, the Mucinous Cystadenocarcinoma? Ideally, a combination of radiographic imaging (CT), ultrasonography, and needle biopsy and aspiration may be able to confidently identify some patients. The majority of serous cystadenomas are composed of numerous cystic areas, the maximum diameter of any individual cystic area being ≤2 cm and often containing many smaller, occasionally microscopic, cystic areas, thus the name "microcystic adenoma," as coined by Compagno and Oertel.[1] Subsequent studies, however, have found these neoplasms to contain larger cystic areas in 12% to 80% of patients (Fig. 3).[5,6] Other CT findings may be of help in identifying serous cystadenomas, including the presence of calcification (Fig. 4), a sign of a more indolent process, a central scar, the absence of me-

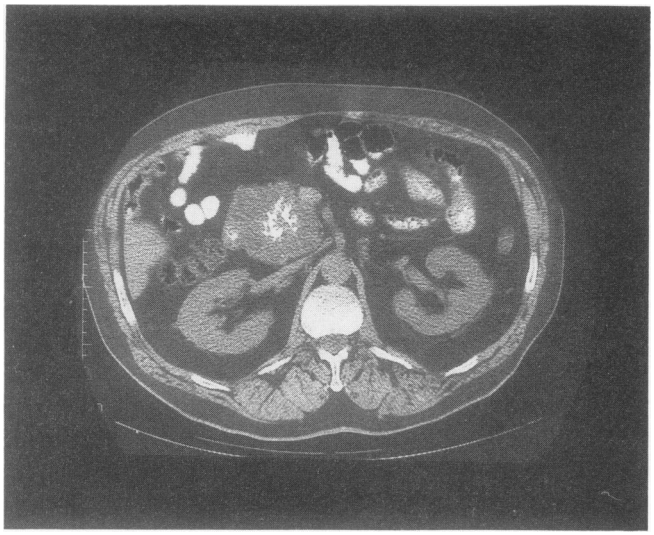

FIG. 4. CT scan showing serous cystadenoma of the head of the pancreas. Note the central stellate calcification.

tastases, and hypervascularity. Using this spectrum of findings, Johnson et al.[6] were able to correctly differentiate in a blinded, retrospective study about 95% of serous cystadenomas from other cystic neoplasms of the pancreas. Differentiation from other cystic lesions, however, such as pancreatic pseudocysts, may not be as straightforward. Warshaw et al.[5,17] found that six of 18 patients with serous cystadenoma were incorrectly diagnosed and treated as a pancreatic pseudocyst and occasionally were managed by cystoenteric drainage. Although none of our patients with serous cystadenomas had initially been treated inadvertently by cystoenteric drainage, we have managed several patients with mucinous cystadenocarcinomas so treated (unpublished data). Nevertheless, use of strict criteria of presumed cystic neoplasms of the pancreas[6] in the appropriate clinical setting may be able to differentiate some patients with serous cystadenomas with a fairly high grade of certainty.

Needle biopsy and aspiration as a definitive diagnostic test, as used on two occasions in our study, has several potential pitfalls, including sampling error, lack of characteristic cystic contents, and a small risk of complications such as pancreatitis or tumor seeding along the needle track by carcinomas.[24] Warshaw et al.[5] found that serous cystadenomas had areas of discontinuous epithelium in 40%, although when present, the epithelium was uniformly serous and consistent with its site of origin, the unipotential proximal ductules.[5,25] Conversely, the spectrum of mucinous cystadenoma/cystadenocarcinoma also may have a discontinuous epithelium in 70% and have a lining not entirely constituted of mucinous cells.[26] Such discontinuity and non-uniformity of the surface epithelium may lead to significant potential for sampling error and resultant false-negative biopsy reports. When positive, the characteristic cytology of serous cystadenoma is that of cellular sheets of glycogen-containing low cuboidal cells, clear cytoplasm without vacuoles, and intranuclear cytoplasmic inclusions (Figs. 5 and 6).[1,27]

Analysis of cyst contents also may be of some diagnostic use. Serous cystadenomas are characterized by the absence of mucin[1] and positive immunostaining for the cytoker-

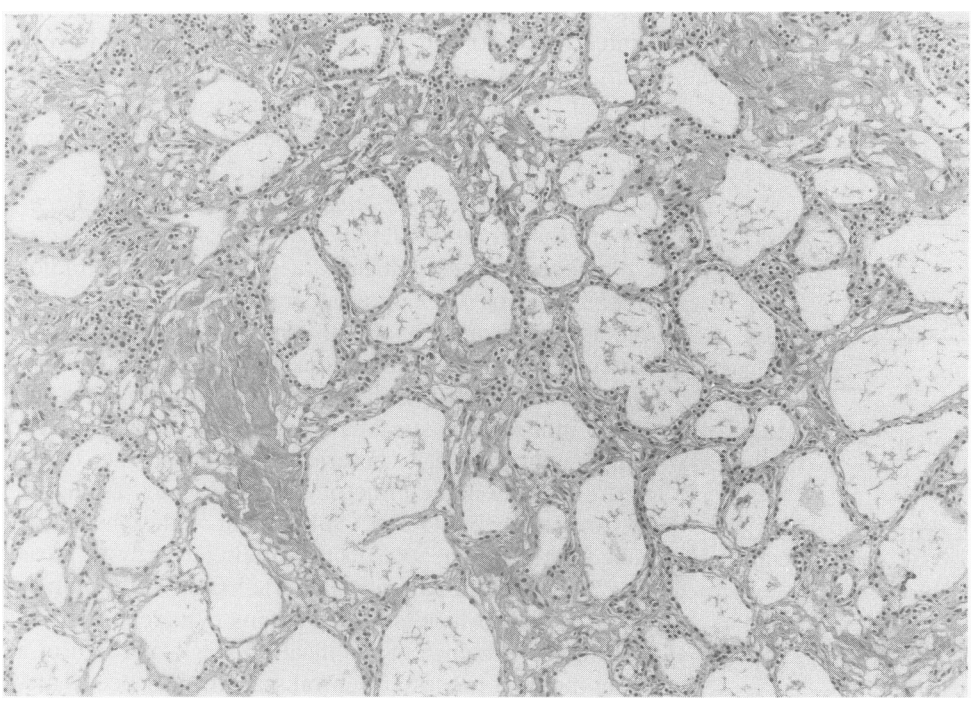

FIG. 5. Pancreatic serous cystadenoma showing cysts containing flocculent material lined by low cudoidal epithelium with dense acellular collagen in their walls.

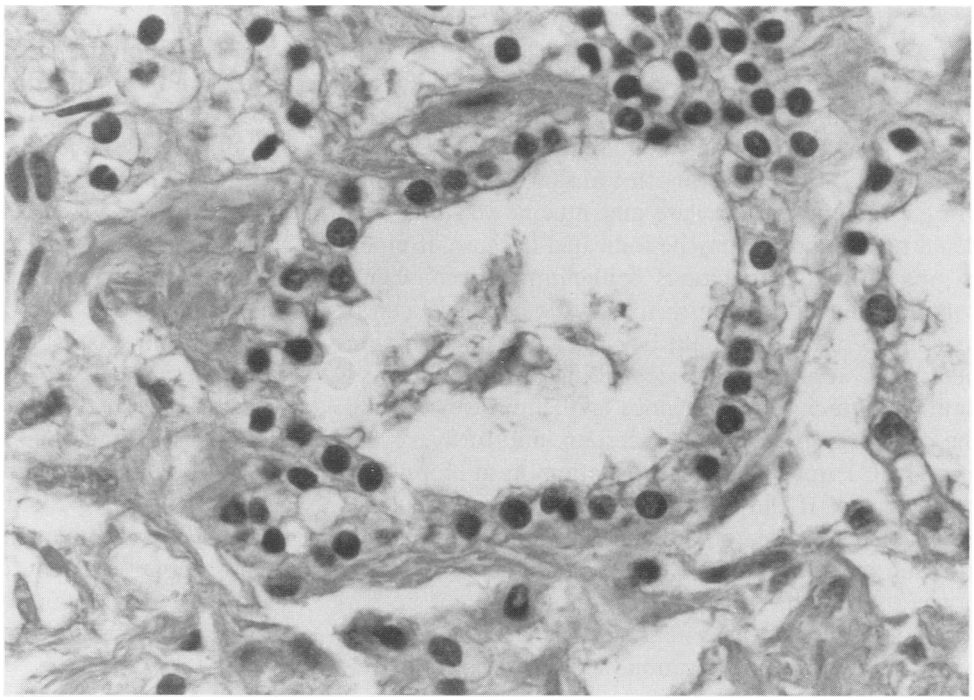

FIG. 6. Detail of serous cystadenoma showing low cuboidal cells with cytologically benign-appearing nuclei and a moderate amount of cytoplasm showing clearing. Some flocculent secretion material is present in the middle of the cyst.

atins AE1 and AE3[28] or positive periodic acid-Schiff (PAS) reaction.[29] Similarly, analysis of the cystic content should not demonstrate an increased concentration of amylase as with pancreatic pseudocysts, increased levels of CA19-9 or CEA (carcinoembryonic antigen) as with pancreatic ductal cancers with cystic necrosis,[28] or mucin as with mucinous cystic neoplasms.

Should All Cystic Neoplasms of the Pancreas Be Resected? Several factors interplay in this decision: the confidence of a preoperative diagnosis of serous cystadenoma *versus* its mucinous counterpart as described above, the clinical presentation and symptoms, the safety of resection, and the potential consequences of nonresective therapy.

Most serous cystadenomas in our experience (27 of 40) were symptomatic and necessitated operative intervention either by resection or biliary or gastric bypass. In contrast, with the ever-expanding use and refinement of imaging techniques, it is likely that more cystic lesions of the pancreas will be found incidentally, many of which will be asymptomatic. Within this context, the safety of resection becomes an important consideration and is based primarily on location of the tumor and the experience of the surgeon. Lesions in the body and tail of the pancreas are easily amenable to distal pancreatectomy with few complications. In contrast, tumors of the head or uncinate process would require a Whipple-type pancreaticoduodenectomy. Enucleation is not a viable option based on the results of our study. Of eight enucleations, there were two postoperative deaths and four complications requiring reoperation (one pancreatitis, one pancreatic pseudocyst, and two pancreatic fistulas). Even though major pancreatic resections have become much safer in centers with considerable experience with pancreatic surgery,[4,10,11] deaths and short- and long-term complications continue to occur after major proximal pancreatic resection, as documented in our experience. With cystic lesions in the head/uncinate process, one must weigh the risks and benefits. In older patients, consideration should be given to bypass-type procedures without formal resection. Two patients in our series with biopsy-proven serous cystadenomas believed too large for safe resection lived 7 and 23 years before dying of unrelated causes. The potential consequences, however, of nonresective treatment include a small risk of malignant transformation,[16] hemorrhage, chronic pancreatitis,[14] recurrent acute pancreatitis, or slow progressive enlargement with the eventual development of obstructive symptoms.

What Is the Appropriate Treatment if a Cystic Neoplasm of the Pancreas Is Found Incidentally During Celiotomy for Another Cause? This situation arose eight times in our experience. Many of the factors discussed above for asymptomatic cystic neoplasms of the pancreas must be considered. Without the benefit of a preoperative CT or ultrasound, it will be difficult to grossly differentiate the serous from the mucinous variety of cystic neoplasms. If the tumor arises in the body or tail of the pancreas, a distal pancreatectomy is warranted without attempts to differentiate the histology because the mortality and short- and long-term morbidity of a distal pancreatic resection is small. In contrast, tumors in the proximal pancreas present a much more difficult decision because of the po-

tential morbidity and mortality rates attendant with proximal pancreatectomy. An open biopsy probably should not be carried out because it could potentially spill tumor cells, and the discontinuity of the epithelial lining might afford an inappropriate confidence in a diagnosis of benignity. In contrast, both transduodenal aspiration of cyst content (for amylase and mucin) and transduodenal needle biopsy may be indicated because, if mucin is present or if a mucinous epithelium is seen, then a confident diagnosis of mucinous cystic neoplasm can be made and resection would be indicated either simultaneously or at a later date, depending on the clinical situation. If mucin or a mucinous epithelium is not found, the diagnosis still remains uncertain, and further evaluation by CT imaging or repeated attempts at biopsy may be indicated. If the tumor is eccentrically located and amenable to enucleation, this may be appropriate for diagnostic purposes only. If a potential pancreatectomy is not planned, however, enucleation should not be performed because of the potential for local tumor seeding with this noncancer operation, should the diagnosis be that of pancreatic malignancy.

Is Serous Cystadenoma a Marker for Other Diseases? Several other authors have described the association of serous cystadenoma of the pancreas with other disorders.[3,12,13,15,18,19] Unlike Corbally and colleagues,[23] we found no strong propensity for unrelated tumors in other organ systems. Coexistent multinodular goiter occurred in four of our patients, however, in accordance with the findings of Soloway,[18] and one papillary carcinoma of the thyroid was found. Montag and associates[12] reported two patients with serous cystadenomas associated with ductal adenocarcinoma of the pancreas, raising the possibility of a common etiopathogenesis affecting the two related cell types; one of our patients had a synchronous ampullary carcinoma that would be consistent with this concept. The von Hippel–Lindau syndrome is well known to be associated with cystic lesions of the pancreas.[19] Although we carefully excluded patients in our series with gross polycystic disease of the pancreas, including those with the polycystic variant of von Hippel–Lindau syndrome, five of the 40 patients in our experience had one or more minor features of the von Hippel–Lindau spectrum: angiolipoma of the kidney, hemangiomatosis of the small intestine, renal cysts, and two pheochromocytomas. The latter neoplasm is itself distinctly uncommon, and with two of 40 patients with serous cystadenoma harboring a pheochromocytoma, this association seems unlikely to be coincidental. In contrast, the apparent association in our experience of cholelithiasis, diabetes mellitus, colonic polyps, and colonic carcinoma with serous cystadenoma, as noted also by others,[3,18,23] is more likely a function of the age of the patients and the propensity of a more complete medical evaluation of these patients rather than a true association between the disease processes.

In summary, the diagnosis of serous cystadenoma should be considered with all cystic lesions of the pancreas. Although these lesions have been relatively unusual in our past experience (40 in 55 years at our institution), increased use and refinement of imaging techniques of the abdomen (and pancreas) may disclose more asymptomatic serous cystadenomas. Provided the clinical presentation and CT appearance is characteristic and an objective diagnosis is obtained histologically, these lesions can be managed expectantly. Symptomatic lesions or those of uncertain diagnosis are best managed with resection, especially when located in the body or tail of the gland. Proximally located serous cystadenomas can be treated by formal pancreatic resection or by biliary/duodenal bypass if too large or too dangerous to resect. We do not recommend enucleation as the definitive treatment in any case. The possibility of associated conditions should be considered.

Acknowledgments

The authors thank M. M. Churchward and D. I. Frank for their help in preparing this manuscript.

References

1. Compagno J, Oertel JE. Microcystic adenomas of the pancreas (glycogen-rich cystadenomas): a clinopathologic study of 34 cases. Am J Clin Pathol 1978; 69:289–298.
2. Howard JM. Cystic neoplasms and true cysts of the pancreas. Surg Clin North Am 1989; 69:651–665.
3. Hodgkinson DJ, ReMine WH, Weiland LH. Pancreatic cystadenoma: a clinicopathologic study of 45 cases. Arch Surg 1978; 113: 512–519.
4. Katoh H, Rossi RL, Braasch JW, et al. Cystadenoma and cystadenocarcinoma of the pancreas. Hepatogastroenterol 1989; 36:424–430.
5. Warshaw AL, Compton CC, Lewandrowski K, Cardenosa G, Mueller PR. Cystic tumors of the pancreas: new clinical, radiologic, and pathologic observations in 67 patients. Ann Surg 1990; 212:432–445.
6. Johnson CD, Stephens DH, Charboneau JW, et al. Cystic pancreatic tumors: CT and sonographic assessment. AJR 1988; 151:1133–1138.
7. Friedman AC, Lichtenstein JE, Dachman AH. Cystic neoplasms of the pancreas: radiological-pathological correlation. Radiology 1983; 149:45–50.
8. Itai Y, Ohhashi K, Furui S, et al. Microcystic adenoma of the pancreas: spectrum of computed tomographic findings. J Comput Assist Tomogr 1988; 12:797–803.
9. Helpap B, Vogel J. Immunohistochemical studies on cystic pancreatic neoplasms. Pathol Res Pract 1989; 184:39–45.
10. van Heerden JA. Pancreatic resection for carcinoma of the pancreas: Whipple versus total pancreatectomy—an institutional perspective. World J Surg 1984; 8:880–888.
11. Crist DW, Sitzmann JV, Cameron JL. Improved hospital morbidity, mortality and survival after the Whipple procedure. Ann Surg 1987; 206:358–365.
12. Montag AG, Fossati N, Michelassi F. Pancreatic microcystic adenoma coexistent with pancreatic ductal carcinoma: a report of two cases. Am J Surg Pathol 1990; 14:352–355.

13. Rosenbaum H, Connolly PJ, Climie ARW, Reveno WS. Pancreatic cystadenoma with intestinal hemorrhage. Am J Roentgenol 1963; 90:735–739.
14. Sarles H, Cambon P, Choux R, et al. Chronic obstructive pancreatitis due to tiny (0.6 to 8 mm) benign tumors obstructing pancreatic ducts: report of three cases. Pancreas 1988; 3:232–237.
15. Doll DC, List AF, Yarbro JW. Evan's syndrome associated with microcystic adenoma of the pancreas. Cancer 1987; 59:1366–1368.
16. George DH, Murphy F, Michalski R, Ulmer BG. Serous cystadenocarcinoma of the pancreas: a new entity? Am J Surg Pathol 1989; 13:61–66.
17. Warshaw AL, Rutledge PL. Cystic tumors mistaken for pancreatic pseudocysts. Ann Surg 1987; 205:393–398.
18. Soloway HB. Constitutional abnormalities associated with pancreatic cystadenomas. Cancer 1965; 18:1297–1300.
19. Horton WA, Wong V, Eldridge R. Von Hippel-Lindau disease: clinical pathological manifestations in nine families with 50 affected members. Arch Intern Med 1976; 136:769–777.
20. Kaplan EL, Meier P. Nonparametric estimation from incomplete observations. J Am Statist Assoc 1958; 53:457–481.
21. Peto R, Peto J. Asymptotically efficient rank invariant procedures (with discussion). J R Statist Soc, Series A, 1972; 135:185–207.
22. Compagno J, Oertel JE. Mucinous cystic neoplasms of the pancreas with overt and latent malignancy (cystadenocarcinoma and cystadenoma): a clinicopathologic study of 41 cases. Am J Clin Pathol 1978; 69:573–580.
23. Corbally M, McAnena O, Urmacher C, Herman B, Shiu M. Pancreatic cystadenoma: a clinicopathological study. Arch Surg 1989; 124:1271–1274.
24. Jones EC, Suen KC, Grant DR, Chan NH. Fine-needle aspiration cytology of neoplastic cysts of the pancreas. Diagn Cytopathol 1987; 3:238–243.
25. Nyongo A, Huntrakoon M. Microcystic adenoma of the pancreas with myoepithelial cells: a hitherto undescribed morphologic feature. Am J Clin Pathol 1985; 84:114–120.
26. Shorten SD, Hart WR, Petras RE. Microcystic adenomas (serous cystadenomas) of pancreas: a clinical investigation of eight cases with immunohistochemical and ultrastructural studies. Am J Surg Pathol 1986; 10:365–372.
27. Young NA, Villani MA, Khoury P, Naryshkin S. Differential diagnosis of cystic neoplasms of the pancreas by fine-needle aspiration. Arch Pathol Lab Med 1991; 115:571–577.
28. Albores-Saavedra J, Angeles-Angeles A, Nadji M, et al. Mucinous cystadenocarcinoma of the pancreas: morphologic and immunocytochemical observations. Am J Surg Pathol 1987; 11:11–20.
29. Cubilla AL, Fitzgerald PJ. Tumors of the exocrine pancreas. Washington, DC: Armed Forces Institute of Pathology, 1984; 100–105.